STATUS REPORT
on
NASA RESEARCH GRANT

26, GRANT NsG-156/47-002-001
For Period 4/1/66 through 9/30/66
Med. C. Virginia

CIRCULATION OF THE BRAIN

Human Cerebrovasodilator Effects of "Pure" Hypoxia.

The completion of the current phase of the investigation of the responses of the cerebral circulation (CBF) to "pure" (eucapnic) hypoxia, begun during the period covered by the last progress report, has been accomplished. The initial portion of this study has been presented in abstract form (see abstract #1).

To observe the effects of pure hypoxia on the cerebral vasculature, sufficient CO_2 must be added to the inspired gas mixture to offset the lowered $PaCO_2$ from the hypoxemic-induced hyperventilation. This was accomplished by the addition of adequate quantities of CO_2 to inspired low oxygen mixtures to maintain the end-tidal CO_2 at control levels. The resulting data indicate that hypoxemia, when unopposed by the cerebral vasoconstrictor action of hypocapnia, is a cerebral vasodilator even at mild levels and becomes a progressively more potent stimulus as hypoxemia deepens. As a final step in each experiment the subjects were allowed to hyperventilate without added CO_2 to demonstrate the combined effect of hypoxia and hypocapnia. There was a decrease in CBF toward but not to control levels confirming that hypoxemic-induced cerebral vasodilation is markedly modified by attendant hypocapnia. A paper presenting these experiments in detail is now in preparation. (A manuscript can be submitted to NASA in the very near future if there is need for it.)

Human Cerebrovascular Response to Induced Hypercapnia and Eucapnic Metabolic Alkalosis.

Studies previously reported by others, notably by Schieve and Wilson (1953)

probe from the High Temperature Instruments Company (Philadelphia) which has been stated by its manufacturers to give reproducible linear responses to flows over a wide range. Preliminary studies have been carried out within vitro systems and during in vivo experiments in the dog. Considerable difficulties have been encountered in achieving reproducible calibration. These problems are related, at least in part, to the extreme temperature sensitivity of the instrument. This requires that blood temperature as well as flow be measured. Work is in progress with the assistance of Dr. Alexander M. Clarke (Biophysics Department, Medical College of Virginia) to redesign the associated electronics in an effort to correct the above problems.

Continuous Measurement of the Cerebral Blood Flow in Rhesus Monkeys.

A study of the feasibility of a chronic preparation to study cerebral blood flow in four Rhesus monkeys has been carried out. The preparation consisted of bilateral vertebral artery ligation, installation of electromagnetic flow meters on both carotids, with an externally controllable ligature on the external carotids. We have concluded that ligation of such a large portion of the arterial systems supplying the brain produces excessive ischemia, at least in some portions of the brain. We have decided, therefore, that in the continuation of this study, the preparation will be changed to ligation of one vertebral and one carotid artery, with placement of electromagnetic flow meters on the other vertebral and carotid.

Mechanism and Pattern of Human Cerebrovascular Regulation After Rapid Changes in Blood CO_2 Tension.

This work, which was described in our last progress report, has since been published in final form. (See publication #1).

CIRCULATION OF THE FOREARM

Effects of Hypercapnia on Human Forearm Blood Vessels.

To further our understanding of the effects of hypercapnia on the cerebral vasculature, comparison of the responses of this vascular bed has been made with that in another, namely the human forearm. The effects of CO_2 breathing on forearm blood vessels were studied in 80 experiments in normal subjects following alpha adrenergic blockade with intra-arterial phenoxybenzamine. In several experiments beta adrenergic blockage was also produced with intra-arterial pronethalol or propranolol. The effects of intra-arterial infusion of isotonic saline with high CO_2 tension on forearm blood vessels were also studied in the intact forearm. During CO_2 breathing or during the infusion of saline with high CO_2 tension forearm vascular resistance showed biphasic changes consisting in an initial slight increase in vascular resistance and a marked delayed decrease in vascular resistance. The delayed decrease in vascular resistance during CO_2 breathing was not modified by beta adrenergic blockade with intra-arterial pronethalol or propranolol. The pronounced decrease in vascular resistance seen in the steady state during CO_2 breathing provides a basis for considering the role of CO_2 in the local regulation of blood flow.

BIBLIOGRAPHY

PUBLICATIONS

1. Shapiro, W., Wasserman, A. J., Patterson, J. L., Jr, Mechanism and pattern of human cerebrovascular regulation after rapid changes in blood CO_2 tension. J. Clin. Invest. 45:6, 913, 1966.

2. Kontos, H. A., Richardson, D. W., and Patterson, J. L., Jr., Effects of hypercapnia on human forearm blood vessels. Am. J. Physiol. 212 (5), 1967. In press.

PAPERS (In Preparation)

1. Baker, J. P., Wasserman, A. J., and Patterson, J. L., Jr., Human cerebral vasodilator effects of "pure" hypoxia.

ABSTRACTS

1. Baker, J. P., Wasserman, A. J. and Patterson, J. L., Jr., Human cerebral vasodilator effects of "pure" hypoxia. Clinical Research 14: 1-38, 1966. Presented before the Southern Section of the American Federation for Clinical Research, New Orleans, Louisiana, January, 1966.

2. Wasserman, A. J., Baker, J. P., and Patterson, J. L., Jr., Hypercapnia: The major regulator in $NaHCO_3$-induced human cerebral vasodilation. Circulation, 34:4, Supp. No. III, 235, 1966.